Clinical and Biochemical Indexes from 2019-nCoV infected patients linked to viral loads and lung injury

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ABSTRACT

The outbreak of the 2019-nCoV infection began in December 2019 in Wuhan, Hubei province, and rapidly spread to many provinces in China as well as other countries. Here we report the epidemiological, clinical, laboratory, and radiological characteristics, as well as potential biomarkers for predicting disease severity in 2019-nCoV-infected patients in Shenzhen, China. All 12 cases of the 2019-nCoV-infected patients developed pneumonia and half of them developed acute respiratory distress syndrome (ARDS). The most common laboratory abnormalities were hypoalbuminemia (ALB), lymphopenia, decreased percentage of lymphocytes (LYM) and neutrophils (NEU), elevated C-reactive protein (CRP) and lactate dehydrogenase (LDH), and decreased CD8 count. The viral load of 2019-nCoV detected from patient respiratory tracts was positively linked to lung disease severity. ALB, LYM, LYM (%), LDH, NEU (%) and CRP were highly correlated to the acute lung injury. Age, viral load, lung injury score, and blood biochemistry indexes, ALB, CRP, LDH, LYM (%), LYM, and NEU (%), may be predictors of disease severity. Moreover, the Angiotensin II level in the plasma sample from 2019-nCoV infected patients was markedly elevated and linearly associated to viral load and lung injury. Our results suggest a number of potential diagnosis biomarkers and angiotensin receptor blocker (ARB) drugs for potential repurposing treatment of 2019-nCoV infection.

INTRODUCTION

In December 2019, a cluster of pneumonia cases linked to the Wuhan seafood wholesale market were reported and found to be caused by 2019 novel coronavirus (2019-nCoV), the seventh member of the coronavirus family that infect humans (C. Huang et al. 2020; Li et al. 2020; Tan WJ 2020). A possible person-to-person spread was identified when a cluster of 2019-nCoV patients with Wuhan traveling records emerged in more cities in China(Li et al. 2020)(C. Huang et al. 2020). By Feb. 2nd of 2020, 11901 cases were laboratory confirmed and 259 death. All patients had the novel coronavirus infected pneumonia (NCIP). The novel coronavirus belongs to lineage B of the genus beta-

coronavirus of the Coronavirus family, which includes SARS-CoV and MERS-CoV (Zhu et al. 2020). The 2019-nCoV is the seventh member of the coronavirus family to infect humans (Chan et al. 2020). A recent study reported that fever, cough, myalgia or fatigue were common symptoms, and sputum production, headache, haemoptysis, and diarrhea were less common symptoms (C. Huang et al. 2020). All patients had pneumonia and about half developed dyspnea. One third of the patients were admitted to ICU and 15% died (C. Huang et al. 2020). Compared with the 10% fatal rate of SARS-CoV (Jiang et al. 2005) and 37% fatal rate of MERS-CoV (Niu et al. 2018), 2019-nCoV is now the third lethal virus in the coronavirus family.

Our study describes the clinical characteristics of 12 2019-nCoV infected patients. All patients were admitted to the Shenzhen Third people's Hospital, China. Clinical characteristics and blood biochemical indexes of 2019-nCoV patients were recorded and examined at the hospital. Patient respiratory samples, including throat swabs and bronchoalveoar lavage fluid (BALF), were collected and real-time PCR was used to confirm 2019-nCoV infection. We identified potential biomarkers of disease severity. Our results should help physicians to diagnose and treat patients infected with 2019-nCoV.

RESULTS

Twelve patients (4 females and 8 males) were admitted to Shenzhen Third People's hospital and confirmed to be infected with 2019-nCoV by Guangdong CDC as of Jan 21, 2020. Of these patients, 7 patients were over 60 years old. Notably, one adolescent case (case 7, 10-year-old) was also found. Except for case 5 who lived in Shenzhen, eleven cases (91.7%) lived or traveled to Wuhan city, and two family clusters were identified. Cases 1, 2, 6 and 7 within one family stayed in a hotel at a distance of about 2.5 miles away from Huanan seafood market for 6 days. On Dec 31, 2019 and Jan 1, 2020, they went to two local households for dinner. Cases 1, 2, and 6 developed fever on Jan 1, 2020, and case 6 also developed diarrhea. On Jan 4, 2020, they returned to Shenzhen city (Figure 1) where they lived with case 5, who subsequently developed

fever, cough and myalgia on Jan 8, 2020. Of note, none of the family members had an exposure history to indicate direct contact with seafood, live poultry, or other wild animals. Cases 10 and 11 were a couple who lived about 5.5 miles away from Huanan seafood market. They developed symptoms with fever and cough on Jan 4, 2020, and went to Shenzhen on Jan 13, 2020 (Figure 1). According to the possible exposure histories of the 12 patients, the estimated incubation period ranged from 1 to 13 days. Most of the cases developed influenza-like symptoms, and the intervals between illness onset to admission were between 5 and 16 days (Table 1). Six (50%) cases had underlying diseases, including chronic heart disease, renal diseases, and diabetes. Pneumonia was the most common applications, followed by acute respiratory distress syndrome (ARDS) (including two cases with severe ARDS). All the patients received anti-viral (Ribavirin and Interferon) treatments, and six of them required mechanical ventilation, among whom cases 2, 4 and 10 received invasive mechanical ventilation. Corticosteroids and immunoglobulin were also used in cases 2, 4 and 10 (Table 1).

The complete blood count and blood biochemistry were measured for each patient either on the date of hospital admission, or at the earliest time-point thereafter. The most common laboratory abnormalities noted were hypoalbuminemia, lymphopenia, decreased percentage of lymphocytes and neutrophils, elevated C-reactive protein (CRP) and lactate dehydrogenase (LDH), and decreased CD8 count. (Table 2). The chest computed tomography (CT) scans of all patients showed ground-glass opacity around the shadow and pleural effusion, especially the lower and peripheral parts of the lungs (Figure 2; Figure S1 in Supporting Information). During the progression of the disease, the density of ground-glass opacity increased, and the range became larger, diffusing to the center and finally throughout the lungs (Figure 2). Case 4 developed fulminant myocarditis five days after illness onset. The biochemistry indexes associated with the function of heart, i.e., creatine kinase (CK), myoglobin (MYO), cardiac troponin 1 (Ctn1), brain natriuretic peptide (BNP) and CK myocardial band (CK-MB), were significantly elevated in case 4 (Table 2), and ultrasonic cardiogram results showed that the Left Ventricular Ejection Fraction (LVEF) was 32%, and the Left

Ventricular Diameter (LV) was 61 mm on Jan. 15, 2020 (5 days after illness onset) (Figure S2 in Supporting Information).

We used the Spearman correlation coefficient to calculate the correlation between 2019-nCoV virus cycle threshold (Ct) value, which is reciprocal to virus load, with clinical disease severity scores, APACHE II, partial pressure of arterial oxygen (PaO_2) / fraction of inspired oxygen (FiO_2) ratios, and Murray scores of infected patients (Figure 3A, Figure S3 and Table S1 in Supporting Information). The viral load of 2019-nCoV detected from patients highly correlated with both ARDS index PaO_2/FiO_2 ratio and lung injury Murray score, but not with MODS score APACHE II (Figure 3A; Figure S3 in Supporting Information). This finding is consistent with the clinical features in this report that half of the infected patients developed ARDS and all patients were diagnosed with pneumonia, indicating that lung failure of the infected patients is the major dysfunction caused by 2019-nCoV infection. Using the spearman method, we further correlated the Ct value (viral load) of the 2019-nCoV virus with biochemical and clinical indexes, and found that the levels of infectious diseases indicators ALB, and percentage of immunological cells of LYM, and NEU were significantly correlated with infected 2019-nCoV viral load (Figure 3B).

Among the 8 blood biochemistry indexes distinguished in blood samples of 2019-nCoV infected patients, specifically ALB, CRE, LYM, LYM (%), NEU (%), LDH, CRP, and CD8, we found ALB, LYM, LYM (%), NEU (%), LDH, and CRP were highly linked to lung injury Murray score (Figure 4). Previous studies reported that hypoalbuminemia is a potent, dose dependent predictor of poor outcome (Vincent et al. 2003). Therefore, albumin therapy might be potential remedy for NCIP.

We next statistically analyzed the link between the clinical and biochemical characteristics and disease severity, the definition of which is described in the second edition of medical guidelines of 2019-nCoV infection from the National Health Commission of the People's Republic of China. We calculated the area under the curve

(AUC) of the receiver operating characteristics (ROC) curve for characteristics from 2019-nCoV infected patients. The AUC value of the ROC curve of age was 1, i.e., age could fully predict the disease severity of 2019-nCoV infected patients (Figure 5). The youngest "severe" patient in this Shenzhen cluster was age 56 years old. The amount of 2019-nCoV detected in patients' respiratory tracts and measured conversely in Ct value, as well as the lung injury Murray score and PaO_2/FiO_2 ratio, may very well predict the disease severity (Figure 5). Among the biochemical indexes, the AUC of ROC for the infection and tissue damage indicators, ALB, CRP, and LDH were 1, 0.938, 0.844, respectively, and may also be potential predictors of disease severity. The AUCs for lymphocyte count and the percentage of lymphocytes and neutrophils were 1, 0.844, 0.812 respectively, and thus may also predict disease severity.

A recent article studied the 2019-nCoV genome sequence and predicted that the new coronavirus shared the ACE2 receptor of SARS-CoV(Xintian Xu 2020), which is a critical enzyme in the renin-angiotensin system (RAS) (F. Huang et al. 2014; Zou et al. 2014). RAS plays important roles in maintaining blood pressure homeostasis(Forrester et al. 2018), and salt and fluid balance (Lin et al. 2017). ACE and ACE2 play different roles in RAS; ACE generates Angiotensin II, whereas ACE2 is a negative regulator of the system, decreasing Angiotensin II (Crackower et al. 2002). The abnormal increase of Angiotensin II was reported mostly associated with hypertension and heart failures (Packer and McMurray 2017), and sometimes also lung and renal dysfunctions (Frohlich et al. 2016; Kuba et al. 2005; Zou et al. 2014); (Damman et al. 2018; Imai et al. 2005; Rai et al. 2017; Torres et al. 2014) We measured the plasma level of Angiotensin II from 2019-nCoV infected patients and healthy individuals, the plasma levels of Angiotensin II from 2019-nCoV infected patients were significantly higher than healthy individuals (Figure 6A). Moreover, the level of Angiotensin II in 2019-nCoV patients was strongly-associated with viral load and lung injury (Figure 6B and 6C), suggesting that the imbalanced renin-angiotensin system in patients was caused by 2019-nCoV and drugs of ACEI and ARB balancing RAS may be used repurposing on 2019-nCoV infected patients.

DISCUSSION

We report 12 cases with laboratory confirmed 2019-nCoV infections. All patients were admitted to the Shenzhen Third People's hospital, Shenzhen, China. All patients were either living or traveling to Wuhan from late December of 2019 to early January of 2020, except case 5 who stayed in Shenzhen during the time period. Two family clusters were identified, and case 5 was in one of the family clusters with cases 1, 2, 6, 7. This secondary infection of case 5 is one evidence of possible person-to-person spread of 2019-nCoV. Cases 1, 2, 6, 7 might have been simultaneously infected in Wuhan, probably by a super-spreader contacting them in the hotel or home of their relatives, as five of their relatives in Wuhan developed similar symptoms(Chan et al. 2020). Since case 5 had disease onset 4 days after family members returning from Wuhan, the latency of 2019-nCoV might be as short as 1-4 days while the latency of most other patients was from 7-13 days (Figure 1). Two out of the 12 patients had no diagnosis of fever, including case 7 who had a clinical image check when accompanying family members to the hospital (Table 1). The risk of virus spread increased with non-fever patients, indicating that it is important to establish epidemiological history during clinical reception of the patients.

All samples from the respiratory tract, including throat swabs and BALF were collected from 10 patients. Comparing the laboratory tests of these samples, the results of throat swabs and BALF collected at the same time from case 1, 3 and 4 were not consistent (Table S1 in Supporting Information), i.e., positive in BALF and negative in throat swabs, indicating that BALF was a more reliable sample for the 2019-nCoV test. It's worth noting that the laboratory test of BALF from case 8 was negative, but positive with throat swabs. Case 8 was discharged from our hospital after one week. Further studies are necessary to elucidate whether the foundation of disease was related to the location of the virus in the respiratory tract.

We found that the viral load was crucial in determining the disease severity, especially

strongly correlated with lung injury Murray score (Figure 3A). Notably, the viral load from case 4 was very high when fulminant myocarditis also occurred (Table 2 and Figure 3). This high viral load lasted for one week, indicating that the early detection of high viral load may associated with a high risk of fulminant myocarditis.

Our study provides a list of potential predictors for disease severity. For example, our study demonstrated that ALB and LYM counts were negatively correlated with the Murray scores, while CRP and LDH levels were positively correlated with the Murray scores in patients with 2019-nCoV (Figure 4). The Murray score was originally developed to assess the severity of acute lung injury in ARDS (Murray et al. 1988), and a higher scores indicate greater severity in ARDS patients. This is consistent with previous studies showing that hypoalbuminemia, lymphopenia, and CRP $\geqslant$ 4 mg/dL were the predictive factors for pneumonia progression to respiratory failure in MERS-CoV infected patients and elevated lactate dehydrogenase was found with severe acute respiratory syndrome (SARS-CoV) infection on hospital admission　(Ko et al. 2016) (Liu et al. 2004) (Leem et al. 2018). Therefore, the combinations of the hypoalbuminemia, lymphopenia, and high concentrations of CRP and LDH in 2019-nCoV infected patients upon hospital admission may predict more severe acute lung injury.

We discovered the markedly increased level of Angiotensin II in the plasma samples from 2019-nCoV infected patients. Our previous mice study has demonstrated that SARS-CoV could bind to its receptor ACE2, down-regulating its expressions, resulting increased Angiotensin II level in mice blood samples, signaling through angiotensin II receptor 1, induced acute lung injury (F. Huang et al. 2014; Imai et al. 2005; Zou et al. 2014). We have also reported that avian influenza A virus H5N1 infected mice exhibited the acute lung injury through dysregulating RAS, and markedly elevation of Angiotensin II level in H7N9 infected patients was associated with the disease severity and outcomes (Guo et al. 2015). In addition, a retrospective cohort study in Texas, USA

with hospitalized pneumonia patients reported that prior and inpatients use of ACE inhibitor and ARB were associated with the decreased mortality (Mortensen et al. 2012). Our previous studies demonstrated that ARB drugs, especially losartan could effectively ameliorate mice acute lung injury induced by SARS-CoV and H5N1 influenza virus A (Kuba et al. 2005; Yan et al. 2015). These data suggest that ARB drugs may be used as treatment for ICU patients infected with 2019-nCoV.

The number of laboratory test confirmed patients is rapidly increasing. We hope that this report of the 12 cases in Shenzhen could provide useful information to prepare for potential pandemics of NCIP.

METHODS

Patients

Twelve patients with pneumonia of unknown cause were admitted to the Shenzhen Third People's hospital in Shenzhen, China between Jan 11 and Jan 20, 2020, and were confirmed to be infected with 2019-nCoV by Guangdong CDC (Center for Disease Control and Prevention). The age of the patient ranged between 10 and 72 years old. Of the 12 patients, 3 patients were in a critical condition and 5 were classified as severe, according to the guidelines of 2019-nCoV infection from the National Health Commission of the People's Republic of China. Bronchoalveolar lavage fluid (BALF), and throat swabs samples of 2019-nCoV infected patients were collected to detect virus titers. Blood samples from 2019-nCoV infected patients and healthy individuals working at Shenzhen Third People's Hospital were collected for plasma angiotensin □ levels measurement.

The study was performed in accordance with guidelines approved by the Ethics Committees from Shenzhen Third People's Hospital (SZTHEC2016001), and verbal informed consents were obtained from all patients or patients' family members.

Data collection and analysis of clinical findings

Clinical information, including complete blood counts, blood biochemistry, chest radiographs and computed tomographic (CT) scans from twelve patients with laboratory-confirmed infection of 2019-nCoV were collected at the earliest time-points possible upon hospitalization.

Quantitative reverse transcription polymerase chain reaction

Throat swabs and bronchoalveolar lavage fluid (BALF) were collected from the respiratory tract of the patients at various time-points after hospitalization. Viral RNAs were extracted from samples using the QIAamp RNA Viral Kit (Qiagen, Heiden, Germany), and quantitative reverse transcription polymerase chain reaction (qRT-PCR) was performed using the primers and probes targeting the ORF1ab and N genes of 2019-nCoV as recommended by China CDC (http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html?from=timeline&isappinstalled=0), using a commercial kit specific for 2019-nCoV detection (GeneoDX Co., Ltd., Shanghai, China). The specimens were considered positive if the Ct value was ≤ 38.0, and negative if the results were undetermined. Specimens with a Ct higher than 38 were repeated. The specimen was considered positive if the repeat results were the same as the initial result and between 38 and 40. If the repeat Ct was undetectable, the specimen was considered negative.

Quantification of hypoxia and lung injury

Quantification of hypoxia and lung injury were carried out as previously reported (Bi et al. 2019) (Yang et al. 2019). In brief, the partial pressure of oxygen (PaO_2) in arterial blood taken from the patients at various time-points after hospitalization was measured by the ABL90 blood gas analyzer (Radiometer). The fraction of inspired oxygen (FiO_2) was calculated by the following formula: $FiO_2 = (21 + \text{oxygen flow (in units of l/min)} \times 4)/100$. The PaO_2/FiO_2 ratio (in units of mmHg) was calculated by dividing the PaO_2 value with the FiO_2 value. A PaO_2/FiO_2 ratio less than or equal to 100 mmHg is considered one of the criteria for severe acute respiratory distress syndrome (ARDS).

Plasma angiotensin II measurement

The plasma samples from 12 2019-nCoV infected patients were separated from blood samples in BSL-3 laboratory. The concentrations of plasma angiotensin II were measured by ELISA assay following the manufacturer's instructions (cloud-clone, TX, USA).

Statistical analysis

We used the Mann–Whitney U test to compare between two groups with continuous variables. The Spearman rank correlation coefficient was used for linear correlation analysis between two groups with continuous variables. Receiver operating characteristic (ROC) curves were calculated with area under curves (AUC) estimation for predictive analysis. We considered a P-value less than 0.05 as statistically significant. All the statistical analyses were performed with SPSS 16.0 for Windows (SPSS, Inc.).

Author contributions

L. Liu, C. Jiang, and Y. Liu conceived the project and guided the study. Y. Yang, F. Wang, J. Yuan, Z. Wang, Jingxiu Li, Jianming Li, C. Feng, Z. Zhang, L. Wang, L. Peng

and L. Chen collected clinical samples. Y. Yang and C. Zhang, supervised by C. Zhou, performed the experiments. F. Huang analyzed the biostatistical data with the assistant from C. Zhang, Y. Qin, and D. Zhao. S. Tan, L. Yin and J. Xu provide critical and helpful assistants. C. Jiang, Y. Liu, Y. Yang, C. Zhang, F. Huang, and Y. Qin wrote the manuscript with all authors revised and agreed.

Compliance and ethics

The author(s) declare that they have no conflict of interest.

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FIGURE LEGEND

Figure 1. A timeline of events in human cases with 2019-nCoV.
Patients are ordered in chronological order based on the date of admission to our hospital. Various milestones in the disease course are indicated with different graphics. Patients within a family were marked in red and blue, respectively.

Figure 2. Computed tomographic (CT) scans and Chest radiographs of case 2.
(A) CT scans and (B) chest radiographs of case 2 taken at indicated date were shown. d.a.o: days after illness onset.

Figure 3. The Ct value of virus are highly correlated with clinical and laboratory manifestations in 2019-nCoV-infected patients.
The Ct value of virus is highly correlated with (A) PaO_2/ FiO_2 ratio, Murray score and (B) CRP, ALB, LYM (%), LYM, NEU in 2019-nCoV-infected patients. The Ct value were detected available in 10 patients with 2019-nCoV infection. PaO_2/ FiO_2 ratio, Murray score, ALB, LYM (%), LYM, NEU, CRP and LDH were detected from 12 2019-nCoV-infected patients. Spearman rank correlation analysis (r) and P value are provided in each graph.

Figure 4. Murray score are highly correlated with laboratory manifestations in 2019-nCoV-infected patients.
(A) The Murray score is highly correlated with ALB, LYM, LDH, LYM (%), NEU (%), and CRP. Murray score, ALB, LYM, LDH, LYM (%), NEU (%), and CRP were detected from 12 2019-nCoV-infected patients. Spearman rank correlation analysis (r) and P value are provided in each graph.

Figure 5. Receiver operating characteristic (ROC) curve of clinical and biochemical indicators of 2019-nCoV-infected patients.
(A) ROC curve of the age, Murray score, Ct value of 2019-nCoV, PaO_2/ FiO_2 ratio and (B) ROC curve of the ALB, LYM, CRP, LYM (%), LDH and NEU (%) were calculated between 4 mild 2019-nCov-infected patients and 8 severe 2019-nCov-infected patients. Detailed information is shown in Table 1 and Table 2.

Figure 6. Plasmas angiotensin II levels are increased in 2019-nCoV-infected patients and correlated with viral Ct value and PaO_2/ FiO_2 ratio
(A) Box plot of angiotensin II levels in plasma of healthy controls (n=8) and 2019-nCov-infected patients (n=12). *** P<0.001 (Mann–Whiney U test). The correlation analysis between plasmas angiotensin II levels and (B) viral Ct value, or (C) PaO_2/ FiO_2 ratio of patients with 2019-nCoV infection. The viral titers were detected available in 10 patients with 2019-nCoV infection. PaO_2/ FiO_2 ratio were detected from 12 2019-nCoV-infected patients. Spearman rank correlation analysis (r) and P value are provided in each graph.

Figure S1. Computed tomographic (CT) scans of human cases with 2019-nCoV.

CT scans of cases 1 and 3-12 taken at indicated date were shown.

Figure S2. Assessment of the myocardial function in case 4.
(A-B) The ultrasonic cardiogram results. (C) the Left Ventricular Ejection Fraction (LVEF), and the Left Ventricular Diameter (LV) at the indicated date.

Figure S3. The correlation between APACHE II scores and viral Ct value in 2019-nCoV-infected patients.
The viral titers were detected available in 10 patients with 2019-nCoV infection. APACHE II scores were detected from 12 2019-nCoV-infected patients. Spearman rank correlation analysis (r) and P value are provided in graph.

Table 1. Epidemiological and clinical features of human subjects hospitalized with 2019-nCoV infection.

Table 2. Clinical Characteristics and laboratory results of subjects hospitalized with 2019-nCoV infection.

Table S1. The Ct values of different sample types from the same case determined by qRT-PCR.
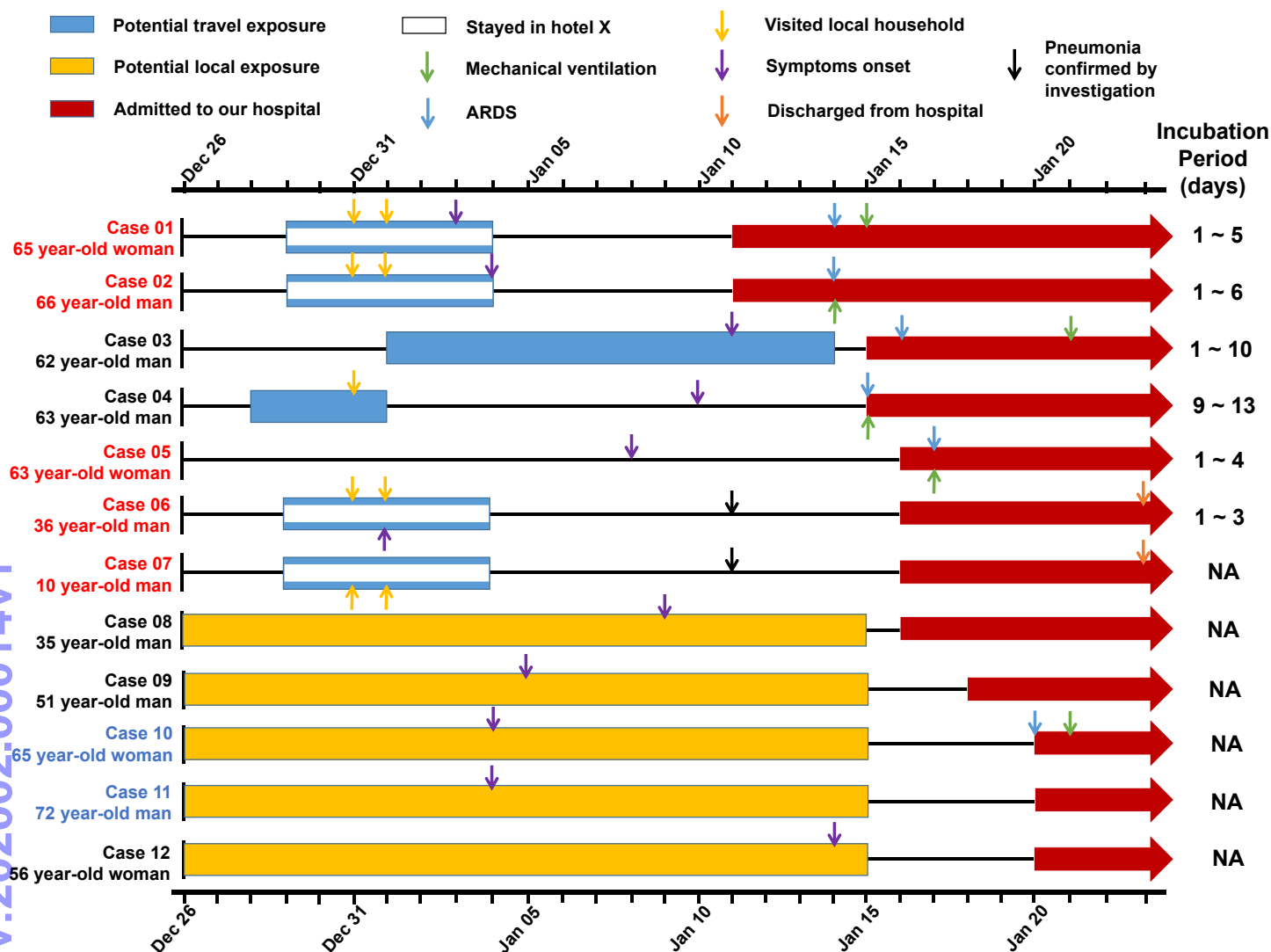
Figure 1

Table 1. Epidemiological and clinical features of human subjects hospitalized with 2019-nCoV infection.

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
Age	65	66	62	63	63	36	10	35	51	65	72	56
Male	Female	Male	Male	Male	Female	Male	Male	Male	Male	Female	Male	Female
Onset to admission (days)	9	8	4	5	8	5	5	7	13	16	16	7
Initial symptoms												
Fever	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes
Cough	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Headache	No	No	No	No	No	No	No	No	No	No	No	No
Myalgia	Yes	Yes	No	No	Yes	No	No	No	Yes	No	No	No
Chill	Yes	Yes	Yes	No	Yes	No	No	No	Yes	No	No	No
Nausea or vomiting	No	Yes	No	No	No	Yes	No	No	No	No	No	No
Diarrhea	No	No	Yes	No	No	Yes	No	No	No	No	No	No
Underlying diseases												
Chronic heart disease	Yes	Yes	Yes	No	No	No	No	No	No	No	Yes	No
Chronic lung disease	No	No	No	Yes	No	No	No	No	No	No	No	No
Chronic renal disease	No	No	Yes	No	No	No	No	No	No	No	Yes	No
Chronic liver disease	No	No	No	No	No	No	No	No	No	No	No	No
Diabetes	No	No	No	No	No	No	No	No	No	Yes	No	Yes
Hypertension	Yes	Yes	No	No	No	No	No	No	No	No	Yes	No
Cancer	No	No	No	No	No	No	No	No	No	No	No	No
Bacterial co-infections	No	Yes	No	Yes	No	No	No	No	No	No	No	No
Complications												
Pneumonia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ARDS	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Severe ARDS	No	Yes	No	Yes	No	No	No	No	No	Yes	No	No
Respiratory failure	No	Yes	No	Yes	No	No	No	No	No	Yes	No	No
Hepatic insufficiency	No	Yes	No	Yes	No	No	No	No	No	No	No	No
Renal insufficiency	No	Yes	No	Yes	No	No	No	No	No	No	No	No
Cardiac failure	No	No	No	Yes	No	No	No	No	No	No	No	No
Shock	No	No	No	Yes	No	No	No	No	No	No	No	No
Treatment												
Antiviral agents	Oseltamivir Ribavirin Interferon	Oseltamivir Ribavirin Interferon	Oseltamivir Ribavirin Interferon	Oseltamivir Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon	Ribavirin Interferon
Corticosteroid	No	Yes	No	Yes	No	No	No	No	No	Yes	No	No
Mechanical ventilation	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Invasive mechanical ventilation	No	Yes	No	Yes	No	No	No	No	No	Yes	No	No
Immunoglobulin	No	Yes	No	Yes	Yes	No	No	No	No	Yes	No	No

Severe ARDS: $PaO_2/FiO_2 < 100$

Table 2. Clinical Characteristics and laboratory results of subjects hospitalized with 2019-nCoV infection.

	Normal range	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
PaO2/FiO2	400-500	131	96	159	65	256	438	469	561	420	126	249	386
WBC (× 10^9/L)	3.5-9.5	4.31	5.24	3.85	6.79	6.71	13.55	6.72	4.62	4.94	5.89	4.99	3.98
LYM (%)	20-50	20.4	23.1	21.6	3.8	11.5	17.5	56.4	34.4	29.4	7.1	19.8	20.9
LYM (× 10^9/L)	1.10-3.20	0.88	1.21	0.83	0.26	0.77	2.37	3.79	1.59	1.45	0.42	NA	0.83
NEU (%)	40-75	72.6	67.4	58.7	93	80.9	77.4	33.7	56.8	64.3	90.9	74.8	75.3
NEU (× 10^9/L)	1.8-6.3	3.13	3.53	2.26	6.31	5.43	10.49	2.26	2.62	3.18	5.35	3.73	3
PLT (× 10^9/L)	100-300	161	118	121	119	215	250	196	236	184	118	99	152
AST (U/L)	0-45	26.7	33.6	26	107	26.2	29.3	34.7	28.9	37.7	52	42.1	36.1
ALT (U/L)	0-45	26.6	26.5	26	62	45.3	30	32.8	22.4	39.5	15.7	29	23.6
TB (umol/L)	3.0-22	10.8	9.5	9.1	6.2	11.6	12	8.5	7.8	7.8	8.4	9.6	5.9
ALB (g/L)	40.0-55.0	36.8	39.5	41.6	35.1	38.3	48.9	46.4	43.4	46.2	34.6	42.6	38.4
CRE (μmol/L)	58-110	46.5	81.9	104	220	44.1	79.7	53	95.4	82.5	54.1	122	43.6
BUN (mmol/L)	3.2-7.1	2.87	5.37	5.51	9.81	4.8	6.65	7.65	4.21	3.71	4.48	6.89	3.12
CK (U/L)	50-310	46	118	97	876	NA	111	70	NA	NA	NA	NA	NA
MYO (ng/mL)	0-110	25.2	38.66	50.1	390.97	32.7	35	18.7	20.5	27	40.1	111.9	23.7
CtnI(ug/mL)	0-0.1	0.012	0.012	0.012	11.37	0.012	0.012	0.012	0.012	0.012	0.014	0.012	0.012
BNP (pmol/L)	0-23.1	4.32	5.7	3.78	161.99	NA	NA	NA	NA	NA	NA	NA	NA
CK-MB(ng/mL)	0-2.37	0.24	0.48	<0.22	20.53	<0.22	0.25	0.26	<0.22	<0.22	0.23	0.97	<0.22
LDH (U/L)	114.0-240.0	662	593	169	720	696	491	475	558	476	1266	510	648
CRP (mg/L)	<10	52.6	38.6	52.95	89.94	53.6	5.8	< 5	35.6	13	33.2	85	28.4
PCT (ng/mL)	0-0.5	0.048	0.04	0.095	9.18	0.031	<0.020	<0.020	0.029	<0.020	0.077	0.218	0.033
CD4 (count/μl)	34-52	47.3	45.8	41.2	18.7	30.9	NA	NA	NA	50.2	34.9	50.7	43
CD8 (count/μl)	21-39	16.7	16.5	11.6	10.9	23	NA	NA	NA	24.9	14.3	17	17.4
CD4/CD8	0.9-3.6	2.83	2.78	3.56	1.72	1.34	NA	NA	NA	2.02	2.45	2.98	2.47

NA: Not available.

Figure 2

A

B

8 d.a.o   13 d.a.o   16 d.a.o
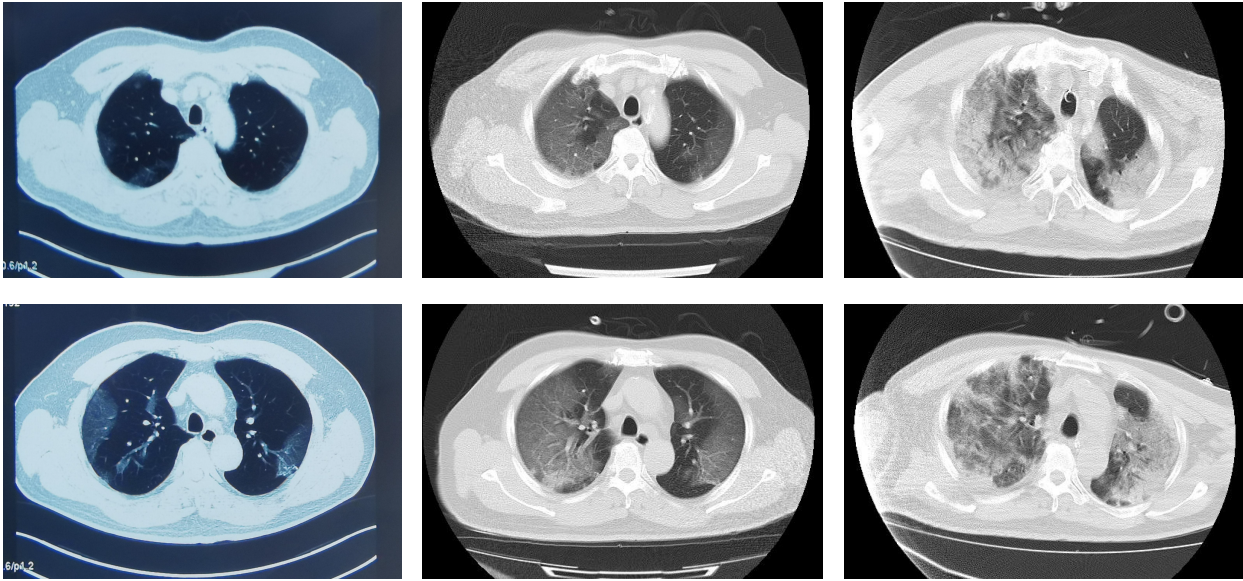
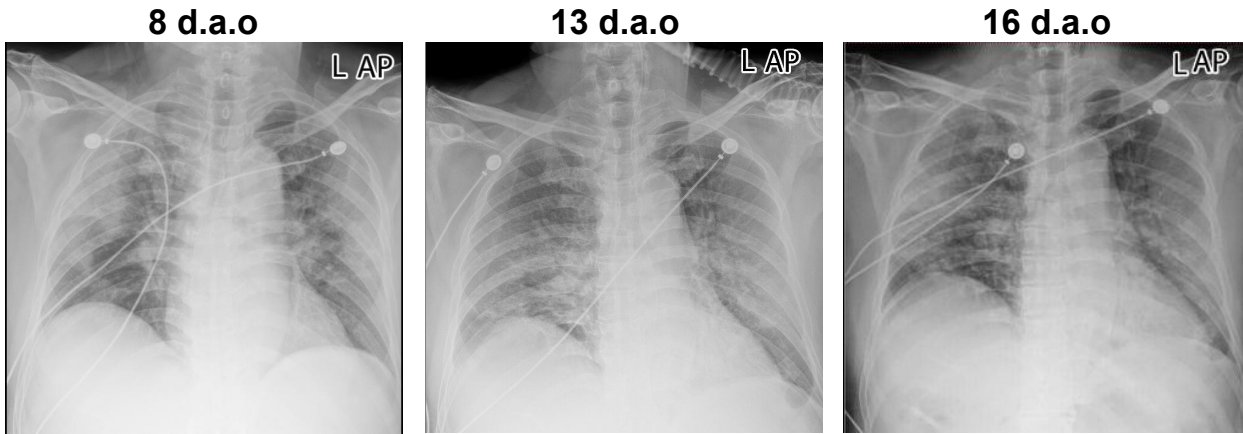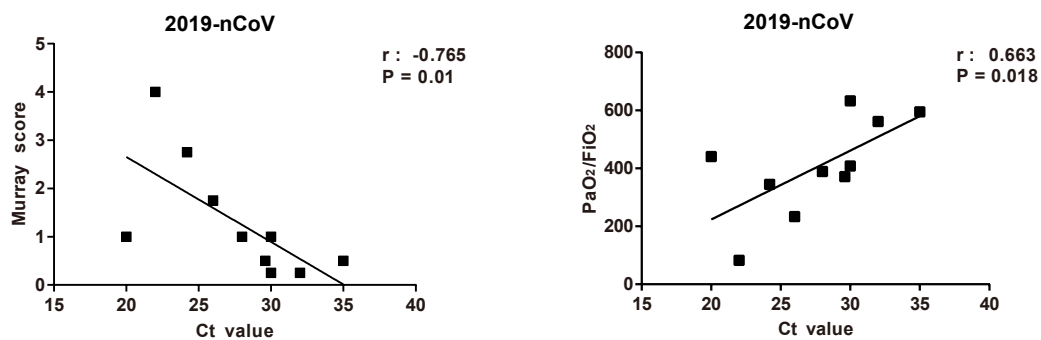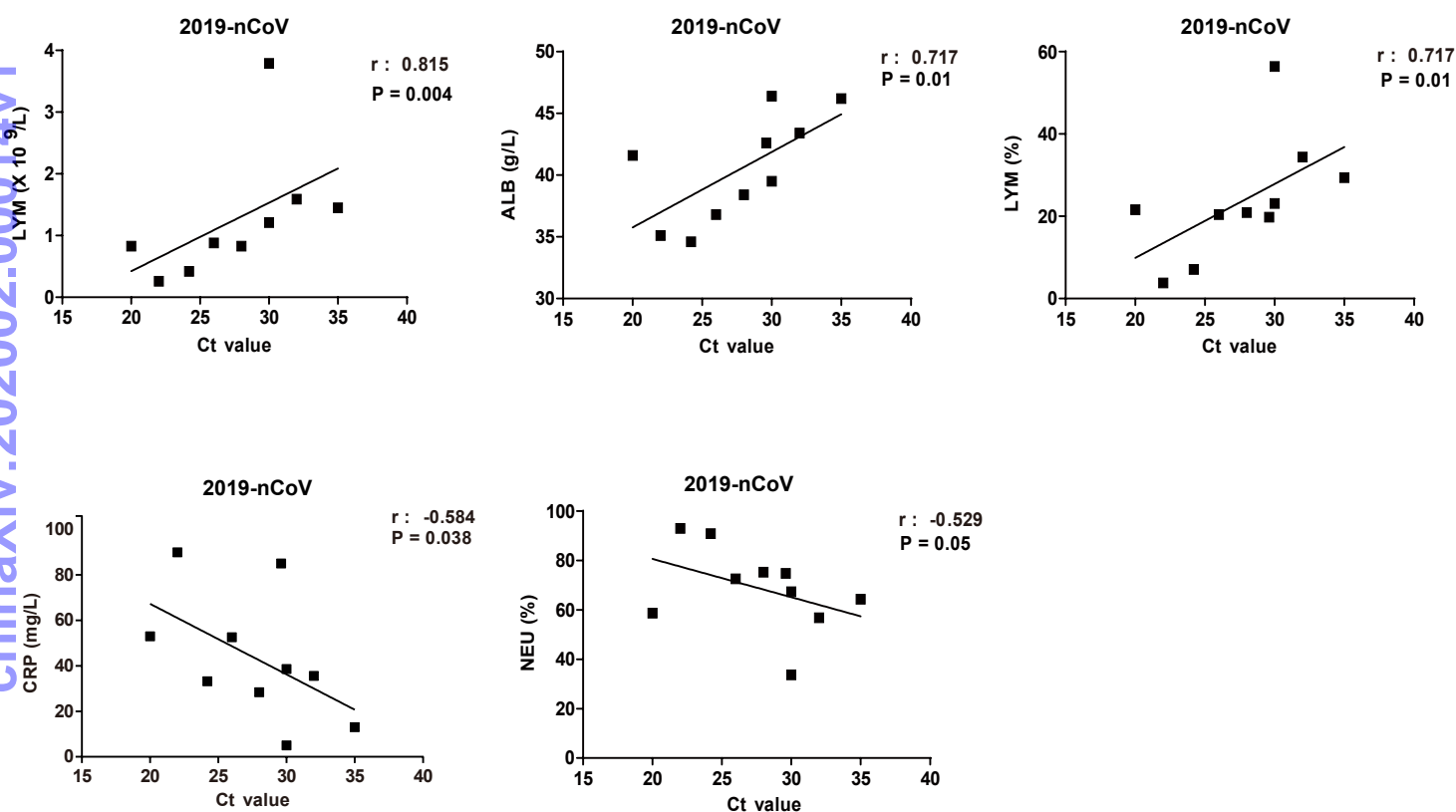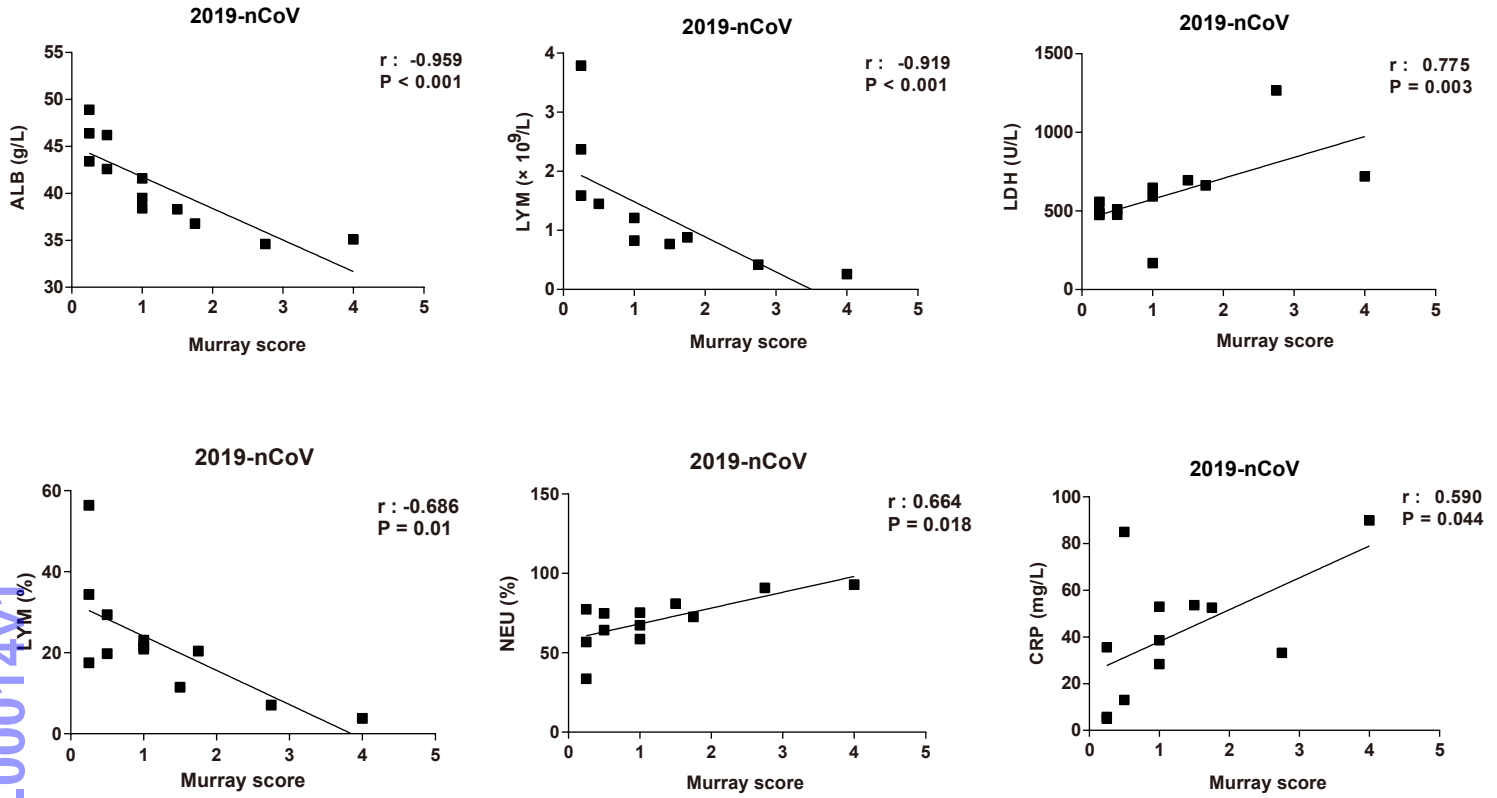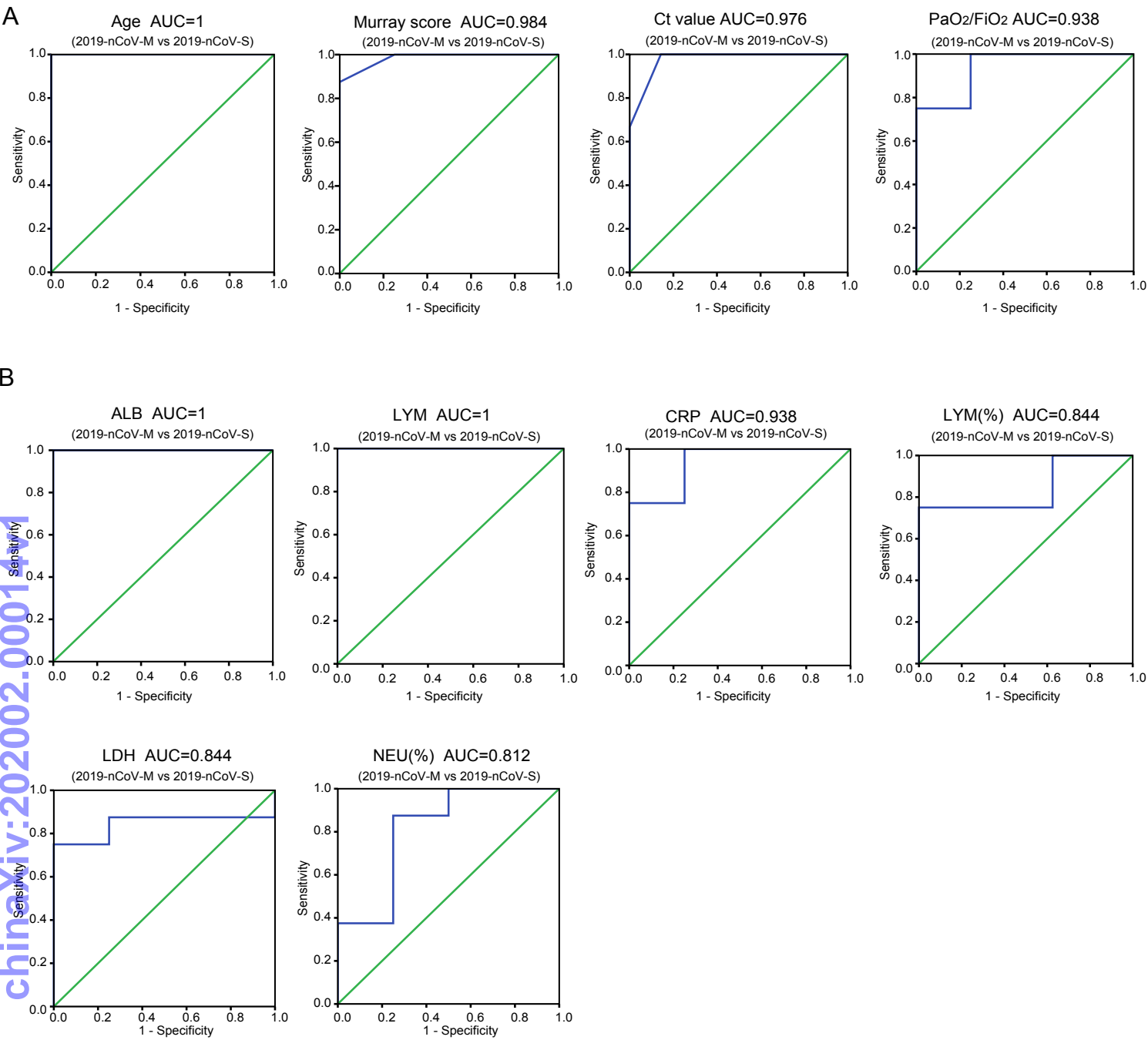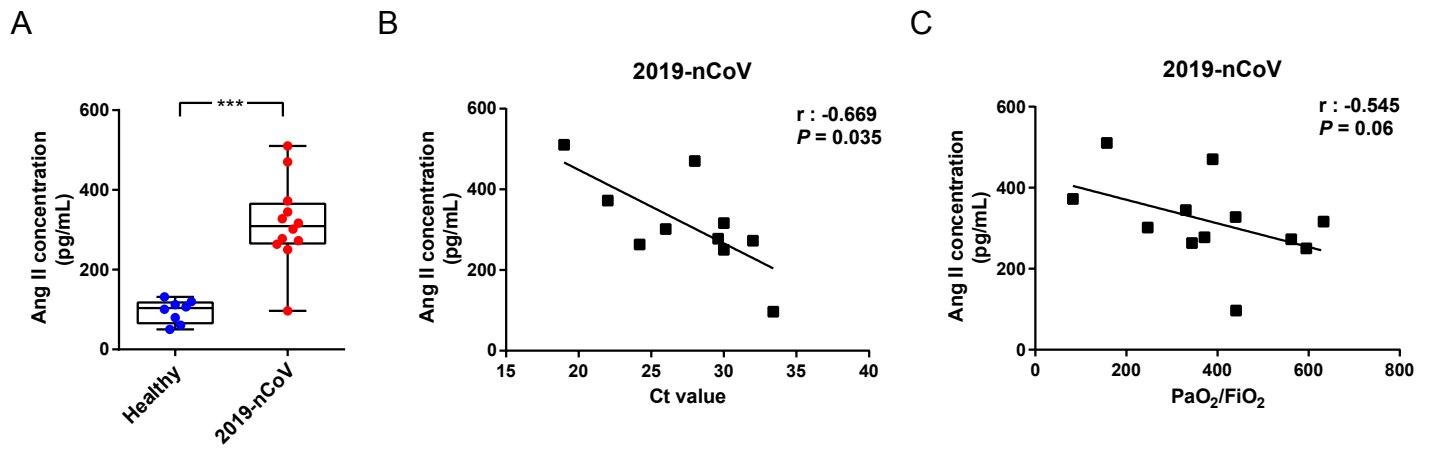# Figure 3

Figure 4

Figure 5

Figure 6

Table S1. The Ct values of different sample types from the same case determined by qRT-PCR

Case No.	Sample collection date (d.a.o)	Ct Values	
		Swab	BALF
1	9	U	26.3
2	8	33.5	19.2
3	11	U	26.5
4	12	U	27.2
8	10	32.5	U

U: Undetected
d.a.o: Days after illness onset
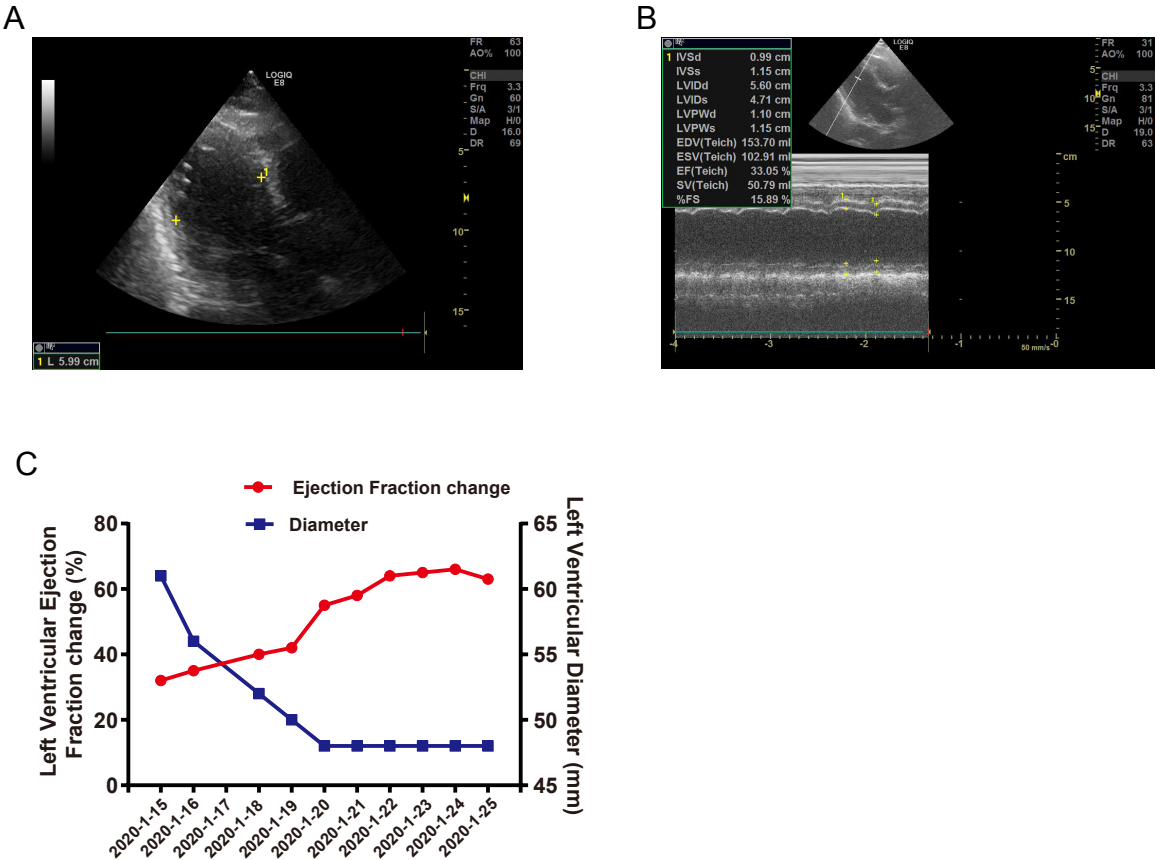BALF: Bronchoalveolar Lavage Fluid

Figure S1

Figure S2

A

B

IVSd	0.99 cm
IVSs	1.15 cm
LVIDd	5.60 cm
LVIDs	4.71 cm
LVPWd	1.10 cm
LVPWs	1.15 cm
EDV(Teich)	153.70 ml
ESV(Teich)	102.91 ml
EF(Teich)	33.05 %
SV(Teich)	50.79 ml
%FS	15.89 %

C

Figure S3

2019-nCoV

r : -0.503
P = 0.08

APACHE II

Ct value